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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte KARL-HEINZ WOELLER, LUDGER KOLBE, CATHRIN SCHERNER, and RAINER WOLBER[1]

Appeal 2016-004051
Application 13/499,861
Technology Center 1600

Before RICHARD M. LEBOVITZ, RICHARD J. SMITH, and RACHEL H. TOWNSEND, *Administrative Patent Judges*.

TOWNSEND, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a self-adhesive transdermal therapeutic system, which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm. However, as to claims 50 and 51, because our affirmance relies on somewhat different reasoning from the Examiner's, we designate our affirmance of the rejection of claims 50 and 51 as New Grounds of Rejection.

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[1] Appellants identify the Real Party in Interest as Beiersdorf AG. (Appeal Br. 3.)

STATEMENT OF THE CASE

Melanin "brings about a more or less pronounced brownish to brown-black skin color." (Spec. 1.) "Problems with hyperpigmentation of the skin have a wide variety of causes and/or are accompanying phenomena of many biological processes." (*Id.* at 2.) Active ingredients and preparations which counteract skin pigmentation are known. (*Id.* at 3.) 4-n-Butylresorcinol is known to inhibit the production of melanin. However, the compound itself "has a tendency to discolor - and to discolor cosmetic or dermatological preparations comprising it." (*Id.* at 4.) Appellants' invention is directed to a system to deliver 4-n-butylresorcinol transdermally and "provide remedies for the disadvantages of the prior art." (*Id.*)

Claims 28–30, 32–35, 37–45, and 49–51 are on appeal. Claim 28 is representative and reads as follows:

> 28. A transdermal therapeutic system, wherein the system comprises 4-n-butylresorcinol as an active ingredient in an amount from 0.001 % to 10 % by weight based on a total weight of the system and is present in a form of a matrix system comprising a self-adhesive matrix that comprises the 4-n-butylresorcinol and is selected from nonpolar polyisobutylene matrices and polar water gel matrices based on agar agar/polyacrylic acid.

(Appeal Br. 22.)

The following grounds of rejection by the Examiner are before us on review:

1. Claims 28, 38, 39, 48, 49, and 51 under 35 U.S.C. § 103(a) as unpatentable over Woeller[2] and Torihara.[3]
2. Claims 28–30, 32–34[4], 41, 44, and 50 under 35 U.S.C. § 103(a) as unpatentable over Wang[5] and Torihara.
3. Claims 35, 37, 42, and 43 under 35 U.S.C. § 103(a) as unpatentable over Wang, Torihara, and Panigrahi.[6]
4. Claim 40 under 35 U.S.C. § 103(a) as unpatentable over Woeller, Torihara, and Panigrahi.
5. Claim 45 under 35 U.S.C. § 103(a) as unpatentable over Woeller, Torihara, and Wang.

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[2] Woeller et al., US 7,829,099 B2, issued Nov. 9, 2010. The application that issued as Woeller '099 was filed June 22, 2005, and published Dec. 22, 2005.

[3] Torihara et al., US 4,959,393, issued Sept. 25, 1990.

[4] The Examiner's rejection refers to claims "28–34." (Final Action 5; Ans. 6.) However, the Examiner acknowledges in the Advisory Action dated May 6, 2015, that claim 31 is not rejected (Advisory Action 1), and Appellants' claim Appendix does not include claim 31 as one of the claims on appeal.

[5] Wang et al., US 5,508,038, issued Apr. 16, 1996.

[6] L. Panigrahi et al., *The Effect of pH and Organic Ester Penetration Enhancers on Skin Permeation Kinetics of Terbutaline Sulfate From Pseudolatex-Type Transdermal Delivery Systems Through Mouse and Human Cadaver Skins*, 6(2) AAPS PharmSciTech E167–173 (2005).

DISCUSSION

I. Claims 28, 38, 39, 48, 49, and 51 are obvious from Woeller and Torihara

The Examiner finds that, like the claimed transdermal therapeutic system, Woeller discloses a self-adhesive polymer matrix that can include a pharmaceutical active ingredient up to 15% by weight of the matrix and can be used to topically or buccally administer the active substance. (Final Action 3–4.) The matrix "comprises from 2% to 55% by weight of (a) at least one polymer which forms a gel in water (interpreted as water gel) and the polymer matrix comprises at least one **polyacrylic acid** polymer, at least one of **agar-agar** and carrageenan and glycerin," meeting one of the recited self-adhesive matrix composition of claim 28. (Ans. 5; Final Action 3.) The Examiner further finds that Woeller discloses the gel matrix is applied on a flexible cover layer constructed from a backing material that can be, among other things, a film, nonwoven or woven. (Final Action 3.) The Examiner notes that in a preferred embodiment the backing materials of Woeller "available for selection include polyethylene, polypropylene, polyether-ester copolymers and polyurethane or else natural fibers." (*Id.* at 3–4; Ans. 6.) Woeller is also said to disclose the use of penetration enhancers in the polymer matrix. (Final Action 4.) The Examiner finds that the difference between Woeller and the claimed transdermal therapeutic system is that Woeller does not disclose the matrix contains 4-n-butylresorcinol as the active ingredient. (*Id.* at 4.)

The Examiner finds that Torihara discloses 4-n-butylresorcinol is a skin depigmental agent and that it can be used along with any cosmetic base ordinarily used for skin depigmental agents. (*Id.*) The Examiner concludes

that it would have been obvious to one of ordinary skill in the art to use 4-n-butylresorcinol with the Woeller matrix thereby providing "a constant level of active substance to be maintained in the body over a long period of time," and that there would have been a reasonable expectation of success in combining that active ingredient with the Woeller matrix. (*Id.*)

We agree with the Examiner's factual findings concerning the prior art teachings and conclusion of obviousness. Appellants' arguments that Woeller does not address substance release characteristics at all (Appeal Br. 7–8), that the presence of an active ingredient is optional in Woeller (Appeal Br. 8; Reply Br. 3), that "none of the examples of pharmaceutical active substances which are mentioned in . . . WOELLER shows any structural or other resemblance with 4-n-butyl resorcinol" (Appeal Br. 8), and that Torihara does not "suggest[] that any of the skin depigmental agents mentioned therein can or should be applied in the form of a matrix system" (Appeal Br. 9; Reply Br. 2), are not persuasive to rebut the Examiner's prima facie case of obviousness.

In particular, "[n]on-obviousness cannot be established by attacking references individually where the rejection is based upon the teachings of a combination of references." *In re Merck & Co.*, 800 F.2d 1091, 1097 (Fed. Cir. 1986). The references must be read, not in isolation, but in combination for what they fairly teach as a whole. *Id.* Furthermore, "[i]t is well settled that a prior art reference is relevant for all that it teaches to those of ordinary skill in the art." *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992).

Regardless of the fact that Woeller does not provide any examples where the matrix includes an active pharmaceutical substance, Woeller

teaches the gel matrix taught can be doped "with hydrophilic active substances, or else, in the case of an appropriate solubilizer, with hydrophobic active substances for wound healing or skin care." (Woeller 8:4–9.) Woeller essentially teaches that any active substance for topical application for wound healing or skin care is capable of being added to the disclosed matrix. And, thus, even if true, it is not dipositive that "none of the examples of pharmaceutical active substances which are mentioned in col. 5, lines 24-30 of WOELLER shows any structural or other resemblance with 4-n-butyl resorcinol" (Appeal Br. 8).

Torihara teaches that 4-n-butyl resorcinol is a skin care active substance, i.e., a depigmental agent to restore age spots or freckles to a "normal skin color." (Torihara 1: 9–16.) That Torihara does not teach 4-n-butyl resorcinol provided in a matrix for transdermal delivery is not of import. The rejection is not an anticipation rejection based on Torihara, but rather an obviousness rejection based on the combined teachings of Woeller and Torihara. "As long as some [reason,] motivation or suggestion to combine the references is provided by the prior art taken as a whole, the law does not require that the references be combined for the reasons contemplated by the inventor." *In re Beattie,* 974 F.2d 1309, 1312 (Fed. Cir. 1992.)

As the Examiner noted, Woeller teaches that "transdermal therapeutic systems for delivering active substances into and/or through the skin have been known for a long time and constitute patch-like systems which in particular are doped with drugs" (Final Action 3; Woeller 1:29–32). Such systems provide "time-dependent release" of the drug and amount released

per unit time and the duration of activity of the drug is influenced directly by the composition of the matrix. (Woeller 1:47–54.) Woeller further teaches the benefits of transdermal therapeutic systems, stating that they

> avoid the need for frequently repeated administration and avoid burdening the skin with high concentrations of active substances, and so reduce irritation to the skin, which is unavoidable in the event of repeated administration of liquid and semisolid administration forms. . . .
>
> In summary, the advantages . . . lie in a distinctly improved compliance on the part of users, which is attributable to the simple and rapid administration and to the long-lasting efficacy of transdermal therapeutic systems.

(Woeller 2:4–15.) In light of the foregoing, the Examiner's findings and conclusions are supported by a preponderance of the evidence that it would have been obvious to one of ordinary skill in the art to use the Woeller transdermal therapeutic system, which employs a simple self-adhesive polymer matrix with 4-n-buytl resorcinol as the active ingredient to achieve the advantages of improved user compliance, due to the rapid administration and the long-lasting efficacy of the transdermal therapeutic system. That is so regardless of whether Woeller specifically addresses particular release characteristics, as Woeller generally teaches that transdermal therapeutic systems are beneficial because they provide "time-dependent" drug release, and none of claims 28, 38, 39, 48, 49, or 51 recite a specific release rate. Appellants did not provide evidence that 4-n-butyl resorcinol would not have been reasonably expected to be released from the matrix described in Woeller. Appellants argue that it could not be predicted what the release characteristics would be, but did not establish that it would not be expected to be released at all. (Appeal Br. 8.)

Appellants argue that "WOELLER and TORIHARA are unable to suggest to one of ordinary skill in the art that any of the matrix materials disclosed in WOELLER is far superior to other matrix materials in terms of release of active substance, let alone in terms of release of 4-n-butylresorcinol," and that this unexpected result renders the claimed invention non-obvious. (Appeal Br. 7.) We are not persuaded that Appellants have provided sufficient evidence of unexpected results. First, that Woeller does not mention release rates of the matrix material does not mean Woeller's matrix does not have a release rate. "[A] compound and all of its properties are inseparable; they are one and the same thing." *In re Papesch*, 315 F.2d 381, 391 (CCPA 1963). And, as discussed above, Woeller teaches that matrices used in transdermal therapeutic systems have time-dependent release that is "determined by the composition of the matrix." (Woeller 1:46–51) Second, the mere fact that Woeller does not report the release rate of its matrix does not render the release rates of the claimed polar water gel—a property that results from the composition of the matrix—unexpectedly far superior. "Mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention." *In re Baxter Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991). As the Examiner noted (Ans. 5), the fact demonstrated by Appellants' Specification that a "polar water gel matrix based on agar/agar polyacrylic acid" results in 34% release of active ingredient present in the matrix at 1% after 24 hours (Spec. 5) would appear to be an inherent property of the polar water gel matrix disclosed by Woeller, (*see*, *e.g.*, Woeller 4:20–65), which Appellants did not dispute falls within the scope of the claim.

Second, to the extent there is a difference between the matrix described in the examples in Appellants' Specification and Woeller, we note that "when unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected compared with the closest prior art." *Baxter.*, 952 F.2d at 392. Appellants' Specification provides a comparison of ingredient release of different matrix systems as follows:

> A nonpolar matrix based on synthetic and natural rubber (KA)
>
> A polar wet adhesive film based on polyacrylic acid/polyvinyl alcohol (FKF)
>
> A nonpolar matrix based on a polyacrylic acid copolymer (PAC)
>
> A polar anhydrous gel matrix based on polyacrylic acid/polyvinylpyrrolidone (WFG)
>
> A nonpolar polyisobutylene matrix (PIB)
>
> A polar water gel matrix based on agar agar/polyacrylic acid (WG)

(Spec. 5.) The active ingredient release results after 24 hours when these matrices included 1% of 4-n-butylresorcinol were reported as follows:

Results of the active ingredient release of different matrix systems:

(KA)	(FKF)	(PAC)	(WFG)	(PIB)	(WG)
7.4%	17.8%	18.1%	20.6%	22.2%	34.0%

(*Id.*) Appellants have simply demonstrated that a WG matrix described by Woeller has better release characteristics than other matrices known in the prior art. However, such prior art matrixes as KA, FKF, PAC, and WFG, were not identified as the closest prior art. In the rejection based on Woeller, WG was identified as the prior art matrix; Appellants have not

provided evidence that the result with WG is attributable to anything other than the inherent properties of the WG matrix which is disclosed by Woeller.

Third, Appellants' argument in the brief on Appeal that the 34% release reported in the Specification "is an unexpected result" (Appeal Br. 7) is merely attorney argument, and the Specification does not identify the release result with WG as unexpected in light of Woeller's teaching of using the same matrix material with an active ingredient in a transdermal therapeutic system (*see* Spec. 5). The Specification indicates that "[a] disadvantage of TTS is that usually only ca. 10% to 20% of the active ingredient content of the plaster are released during the application time" but that using WG and 1% 4-n-butylresoricnol provided a greater release than about 10–20%. (Spec. 4–5.) The Specification does not establish that this greater that about 10–20% release would not have been achieved with any of the other active ingredients disclosed in Woeller. Thus, Appellants' argument of "unexpectedness" over the prior art teaching is unsupported by relevant objective evidence, and thus, is insufficient to establish unexpected results. *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995) ("'[i]t is well settled that unexpected results must be established by factual evidence. Mere argument or conclusory statements in the specification does not suffice.' *In re De Blauwe,* 736 F.2d 699, 705 (Fed. Cir. 1984); *see also In re Wood,* 582 F.2d 638, 642 (CCPA 1978) ('Mere lawyer's arguments and conclusory statements in the specification, unsupported by objective evidence, are insufficient to establish unexpected results.')).").

Furthermore, as the Examiner noted, Appellants' evidence provides a single data point for an active ingredient present in an amount of 1%. (Ans.

6.) Appellants do not provide any indication that the 34% release rate over 24 hours would be the same across the claimed range of from 0.001 % to 10 % by weight based on a total weight of the system. Contrary to Appellants argument (Reply Br. 3), it is not the Examiner's burden to explain why it cannot reasonably be assumed that the result would be the same across the entire range. "An examiner bears the initial burden of presenting a prima facie case of obviousness. Once the examiner establishes a prima facie case of obviousness, the burden shifts to the applicant to rebut that case." *In re Kao*, 639 F.3d 1057, 1066 (Fed. Cir. 2011). When unexpected results are proffered by Appellants, Appellants must "provide[] an adequate basis to support the conclusion that other embodiments falling within the claim will behave in the same manner" in order to "establish that the evidence is commensurate with [the] scope of the claims." *Id.* at 1068. One data point is insufficient to "to ascertain a trend in the exemplified data which would allow [one having ordinary skill in the art] to reasonably extend the probative value thereof." *In re Kollman*, 595 F.2d 48, 56 (Fed. Cir. 1979). And Appellants have not offered any reasoning by which one of ordinary skill in the art could reasonably conclude that other embodiments falling within the claimed range, such as the inclusion of a much smaller or much larger percentage of 4-n-butylresorcinol, will release in similar percentages to the 1% exemplified data point. Thus, even were unexpected results established for this one data point, it is not commensurate with the full scope of the claim.

For the foregoing reasons, we are not persuaded that the Examiner erred in rejecting claims 28, 38, 39, 48, and 49 as obvious over Woeller and Torihara.

Claim 51

We agree with Appellants that the Examiner does not explain why the subject matter of claim 51, which depends from claim 50 and requires the thickness of a carrier layer to be "below 100 μm," is obvious just because Woeller teaches that polyurethane is a possible selection for a backing material. However, we agree with the Examiner that claim 51 would have been obvious to one having ordinary skill in the art based on the art cited by the Examiner. As the Examiner noted, Woeller teaches that polyurethane is a known backing material for transdermal delivery systems. (Final Action 3–4.) Moreover, the Examiner apparently presumed that polyurethane with the claimed thickness was known in the art, and we note that the Examiner is correct; polyurethane backings with a thickness below 100 μm were known in the prior art.[7] "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). In light of the fact that backing materials having the claimed thickness were known in

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[7] *See, e.g.*, S. Kandavilli et al., *Polymers in Transdermal Drug Delivery Systems*, Pharm. Tech., 62–80, 76 (2002) (disclosing that CoTran 9701 is a known prior art polyurethane film for use in transdermal drug delivery)). *See also* 3M™ CoTran™ 9701 Backing Specification Sheet, available at http://solutions.3m.com/3MContentRetrievalAPI/BlobServlet?lmd=1219086353000&locale=en_WW&assetType=MMM_Image&assetId=1114279695553&blobAttribute=ImageFile (describing the thickness without a carrier of CoTran 9701 as being 51.8 μm)).

the prior art, and Appellants have not argued that the backing having a thickness below 100 µm provides more than predictable results, we agree with the Examiner that claim 51, is obvious.

Because our rationale differs from the Examiner's, we designate our affirmance a new ground of rejection under 37 C.F.R. § 41.50(b).

II. Claims 28–30, 32–34, 41, 44, and 50 are obvious from Wang and Torihara

Claim 28 is also directed to transdermal therapeutic system that comprises a matrix system of "nonpolar polyisobutylene" rather than polar water gel matrices based on agar agar/polyacrylic acid. The Examiner finds that Wang discloses polyisobutylene adhesives useful in transdermal drug delivery systems, and that the thickness of the adhesive is generally "between about 1 mil (0.0254 mm) and about 15 mil (0.381 mm) when used with a rate-controlling membrane, which overlaps with the range of claim 29" (Final Action 5–6.) Wang teaches that any beneficial agent or compound that can be delivered to produce a beneficial and useful result can be incorporated into the adhesive. (Final Action 6; Ans. 7 (noting that Wang teaches "[i]n its broadest application, the adhesives of this invention can be used in monolithic transdermal delivery devices which comprise a thin film of **the agent dispersed in the adhesive** which is normally provided with a protective, agent-impermeable backing layer (col. 3 lines 18–27.") The Examiner further finds that Wang teaches that the adhesive layer thickness is a result effective parameter. (Final Action 6; Ans. 8 "thickness is also preferably selected so that the adhesive does not contain a substantial amount and preferably less than about 15% of the total amount of agent in

the device, particularly in rate-controlled delivery devices (col. 4 lines 33–44 of Wang).") While Wang does not disclose 4-n-butylresorcinol, the Examiner found that this deficiency is met by Torihara.

The Examiner finds that Torihara discloses 4-n-butylresorcinol is a skin depigmental agent and that it can be used along with any cosmetic base ordinarily used for skin depigmental agents. (Final Action 7.) The Examiner concludes that it would have been obvious to one of ordinary skill in the art to use 4-n-butylresorcinol in the transdermal drug delivery system of Wang in light of the fact that Wang "comprises topical contact of a drug on the skin" and Torihara teaches topical application of 4-n-butylresorcinol" and the combination "would have been no more than the combination of prior art elements to yield predictable results." (Final Action 7–8.)

We agree with the Examiner's factual findings regarding the teachings of Wang and Torihara and conclusion of obviousness.

Appellants' argument that the rejection is in error because "the entire disclosure of WANG relates to devices in which the polyisobutylene is used exclusively as an adhesive, whereas the reservoir material is separate and completely different from the polyisobutylene" (Appeal Br. 11; Reply Br. 4) is not persuasive. Appellants concede that Wang mentions "that the adhesive may function as both the agent reservoir and the adhesive." (Appeal Br. 11; *see also* Wang 3:18–27.) There is no disagreement, therefore, that Wang teaches a matrix as claimed, i.e., that the adhesive is a release rate-controlling adhesive that includes an active ingredient to be released transdermally. That the teaching may be "in passing," does not detract from the fact that it is a relevant teaching to one of ordinary skill in

the art. *In re Inland Steel Co.*, 265 F.3d 1354, 1360 (Fed. Cir. 2001) ("The fact that Irie teaches that annealing in addition to adding antimony produces optimal results does not negate Irie's additional teaching that adding antimony is effective even in non-annealed steel.").

Appellants' argument that Wang is concerned "primarily, if not exclusively . . . with the transdermal delivery of oily, non-polar agents such as nicotine, benztropine, secoverine, dexsecoverine, and arecoline . . . substances which are structurally and chemically completely different from 4-n-butylresorcinol" (Appeal Br. 12) is also unavailing. Wang does not teach that the polyisobutylene adhesive can only be used with oily, non-polar agents; rather, Wang indicates that, unlike some prior art adhesives, the disclosed adhesive is capable of being used with such agents. (Wang 2:6–13, 30–36; 3:8–13.) Wang specifically does not limit the agents that can be included with the matrix noting that they can be:

> any beneficial agent or compound that can be delivered by a device herein to produce a beneficial and useful result. The term includes medicines, organic and inorganic drugs, hormones, nutrients, vitamins, food supplements, and other agents that benefit an animal or human.

(Wang 3:48–53.) Thus, that Wang teaches that the matrix can be used with oily, non-polar agents does not detract from the combination of Wang with active ingredients that are not oily, non-polar agents, e.g., active agents disclosed in Torihara. *Accord Merck & Co., Inc. v. Biocraft Labs., Inc.*, 874 F.2d 804, 807 (Fed. Cir. 1989) ("the fact that a specific [embodiment] is taught to be preferred is not controlling, since all disclosures of the prior art, including unpreferred embodiments, must be considered"). Appellants' argument has thus not established that there would not have been a

reasonable expectation of success of including 4-n-butylresorcinol as the active agent in the Wang polyisobutylene adhesive. "Obviousness does not require absolute predictability of success. . . . For obviousness under § 103, all that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d 894, 903–04 (Fed. Cir. 1988).

Appellants argue that the claims concerning a particular thickness range recited for the matrix (claims 29, 30, 41, and 44) are not rendered obvious by Wang and Torihara because Wang does not disclose a thickness value or range for the "reservoir" that contains the active ingredient for transdermal delivery. (Appeal Br. 12.) This argument is not persuasive because Wang teaches the adhesive can be the reservoir, and discloses that the adhesive layer is generally between about 1 mil (0.0254 mm) and about 15 mil (0.381 mm). (Ans. 8; Wang 4:33–35.) This range is within both the broadly claimed range of 0.15 mm to 1.00 mm of dependent claim 29 and the narrower range of 0.20 mm to 0.50 mm that Appellants argue achieves "a particularly high release" (Appeal Br. 13). Moreover, Wang teaches that the thickness of the layer, as well as its composition, is a result effective variable that is "adjusted such that the adhesive layer does not constitute a significant permeation barrier to the passage of the agent." (Wang 4:35–39.)

Appellants further argue that the thickness range disclosed by Wang is in conjunction with a rate controlling membrane. (Reply Br. 5.) We do not disagree with Appellants. But we note that the relevant claims of Appellants with respect to this rejection do not preclude the presence of such a membrane. Furthermore, Wang teaches the thickness of the adhesive is a results effective variable, and it would have been obvious to vary the

thickness of the matrix layer within the claimed range to optimize "the passage of the agent." (Wang 4:37–39.) "[D]iscovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." *In re Boesch*, 617 F.2d 272, 276 (CCPA 1980). And, "'it is not inventive to discover the optimum or workable ranges by routine experimentation.' *In re Aller*, 220 F.2d 454, 456 (CCPA 1955). Only if the 'results of optimizing a variable' are 'unexpectedly good' can a patent be obtained for the claimed critical range. *In re Antonie*, 559 F.2d 618, 620 (CCPA 1977)." *In re Geisler*, 116 F.3d 1465, 1469 (Fed. Cir. 1997). Appellants have not argued or provided evidence of the criticality of the claimed thickness range or that the range provides unexpected results compared with the closest prior art, i.e., the adhesive matrix of Wang, and in light of the teachings of Wang that indicates that thickness of the adhesive will have an effect on the release/passage of the agent. While Appellants have demonstrated a higher release percentage for a polyisobutylene matrix that is thinner than 0.50, the thickness of Wang's adhesive material is taught to be within this range. Thus, it is also not pertinent to the obviousness analysis that "[n]othing in WANG teaches or suggests that the relationship between release rate and thickness of the matrix (even if different from polyisobutylene) is not approximately linear" (Reply Br. 5).

Appellants' arguments concerning unexpected results regarding the matrix material (Appeal Br. 10–11) are unpersuasive as to the rejection relying on Wang, just as they were with respect to the rejection relying on Woeller. That Wang mentions a nonpolar matrix based on synthetic and natural rubber is a suitable reservoir is immaterial in light of the fact that

Wang also teaches and exemplifies using a polyisobutylene matrix. Appellants' comparative data (set forth in the Specification) regarding different matrices and their release rates when they include 1% active ingredient is insufficient to establish unexpected results. Appellants have simply demonstrated that a PIB matrix described by Wang has better release characteristics than other matrices known in the prior art. However, such prior art matrixes as KA, FKF, PAC, and WFG, were not identified as the closest prior art. In the rejection based on Wang, PIB was identified as the prior art matrix; Appellants have not provided evidence that the result with PIB is attributable to anything other than the inherent properties of the PIB matrix which is the same matrix disclosed by Wang. The recognition of an inherent latent property "does not render nonobvious an otherwise known invention." *Baxter*, 952 F.3d at 392.

Nor do Appellants even provide objective evidence that the observed results are unexpected to one having ordinary skill in the art. Attorney argument is not objective evidence. *See Soni*, 54 F.3d at 750. And the Specification does not identify the release result with PIB is unexpected in light of Wang's teaching of using the same matrix material with an active ingredient in a transdermal therapeutic system (*see* Spec. 5).

For the reasons discussed, we are not persuaded that the Examiner erred in rejecting claims 28–30, 32–34, 41, and 44 as obvious over Wand and Torihara.

Claim 50

Regarding claim 50, Appellants argue that the claimed "carrier material" is "completely different" from the strippable release liner disclosed in Wang to have a thickness of 0.076 mm and that the structure in Example 2 demonstrates that the system of Wang does not "consist of" matrix and carrier material for the matrix. (Appeal Br. 13–14.) The Examiner appears to have agreed that the strippable release liner is not equivalent to the claimed carrier, but the Examiner notes in the Answer that the backing material is (Ans. 8), and Appellants apparently concede the point. (Reply Br. 6 (arguing issues with respect to the backing material).) The Examiner also appears to assert that while Wang is silent about the physical properties of the backing material, suitable materials are well known in the art and at least one of those materials would inherently have the qualities claimed, i.e., transparent to translucent, and having a thickness below 100 μm (0.1 mm). (Ans. 8–9.)

To be inherent, the claimed properties of the carrier must necessarily and inevitably be present in the prior art suitable backing materials. *See, e.g.*, *In re Montgomery*, 677 F.3d 1375, 1379–80 (Fed. Cir. 2012). While the Examiner has not cited references reciting these characteristics for backing materials used in transdermal delivery systems, we agree with the Examiner that such materials were known in the prior art.[8] "The

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[8] *See, e.g.*, US 3,731,683 (Ex. I and II (noting the use of cellophane and mylar sheets as backing material for a transdermal delivery system)); US 4,915,950 (4:37–40 (noting the use of sheet or film of flexible elastomeric material with a thickness between 0.0005 inches (0.0127 mm) to 0.003 inches (0.0762 mm) as backing layer for a transdermal delivery system)).

combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 416 (2007). In light of the fact that backing materials having the claimed properties were indeed known in the art as asserted by the Examiner, and Appellants have not argued that the backing provides more than predictable results, we agree with the Examiner that claim 50 is also obvious.

We are not persuaded by Appellants' argument that claim 50 is not obvious because Example 2 of Wang does not describe a transdermal therapeutic delivery system that "consists of" the matrix and carrier material, i.e., the limitation of claim 48, from which claim 50 depends. Wang teaches that a backing layer is useful in a transdermal therapeutic system to prevent passage of the agent through to the skin and provides support for the system if needed. While Example 2 of Wang describes the use of a backing layer with a release rate-controlling membrane, Wang teaches that the adhesive itself could serve as the release rate-control. (Wang 3:28–29.) Thus, Wang teaches a delivery system that "consists of" the matrix, which serves as a release rate control, and a carrier material as required. In light of this, we agree with the Examiner that claim 50 is obvious from the teachings of Wang and Torihara.

However, because our rationale differs somewhat from the Examiner's, we designate our affirmance a new ground of rejection under 37 C.F.R. § 41.50(b).

III. Claims 35, 37, 40, 42, and 43 are obvious

The Examiner finds that, while neither Woeller nor Wang teach the addition of penetration enhancers generally or isopropyl myristate specifically, the addition of such a known penetration enhancer in the transdermal system of Woeller and Torihara or Wang and Torihara would have been obvious in light of the teachings of Panigrahi. (Final Action 8–11). In particular, the Examiner finds that Panigrahi discloses a transdermal drug delivery system and demonstrates that the addition of a penetration enhancer (which it denotes as "permeation enhancer") assists permeation kinetics, and that isopropyl myristate at 2% provides the greatest benefit of the three ester type enhancers tested. (Final Action 9, 11.) The Examiner concludes that it would be obvious to select isopropyl myristate from this finite number of described penetration enhancers with a reasonable expectation of success. (*Id.*) We agree with the Examiner's factual findings and conclusion of obviousness.

Appellants' argue that the Examiner's rejections of the claims is in error because "the system with which PANIGRAHI is concerned differs significantly from the instant transdermal system" and thus there would be no reasonable expectation of success. (Appeal Br. 15–19.) In particular, Appellants note that (1) the compound to be transdermally delivered is terbutaline sulfate—a salt with a bulky amino substituent and an aliphatic hydroxyl group rather than a nonpolar aliphatic group and (2) the matrix "is completely different," being highly polar salts. (*Id.*) This argument is unpersuasive.

Obviousness exists if there is a reasonable expectation of success, *In re O'Farrell*, 853 F.2d at 903–04, and as discussed above, "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." *KSR*, 550 U.S. at 416. Appellants have not argued that the addition of penetration enhancers generally, or isopropyl myristate in particular, are unpredictable with the two different claimed matrices. Moreover, Woeller teaches that the use of enhancers in transdermal systems to affect the amount of drug released and duration of activity of a drug from a transdermal drug delivery system was known. (Woeller 1:50–57.) While it may be true that Panigrahi's matrix and compound for delivery are different than what is disclosed by Wang, Woeller, and Torihara—Panigrahi, nevertheless, teaches isopropyl myristate is an effective penetration enhancer for an active ingredient in a transdermal delivery system. In light of the foregoing, we find the Examiner has established that one of ordinary skill in the art would have had a *reasonable expectation of success* in using isopropyl myristate as a penetration enhancer in the transdermal therapeutic system

Thus, for the reasons discussed, we are not persuaded that the Examiner erred in rejecting claims 35, 37, 40, 42, and 43 for obviousness over Woeller or Wang, Torihara and Panigrahi.

IV. Claim 45 is obvious

In addition to the arguments Appellants raised regarding the deficiency of the combination of Woeller, Torihara, and Panigrahi, Appellants add that the thickness ranges disclosed in Wang are not of the

matrix because Wang is overall concerned with the active being present in the reservoir and not in the matrix. (Appeal Br. 20.) We do not find this argument persuasive for the reasons discussed above, namely that Wang teaches that the adhesive polymer matrix can include the active ingredient (Wang 3:18–27), a point which Appellants concede (Appeal Br. 11). Consequently, the teachings regarding the adhesive thickness are applicable to an adhesive that includes the active.

Thus, we are not persuaded that the Examiner erred in maintaining the rejection of claim 45 as unpatentable over Woeller, Torihara, Panigrahi, and Wang.

SUMMARY

We affirm the rejection of claims 28, 38, 39, 48, 49, and 51 under 35 U.S.C. § 103(a) as unpatentable over Woeller and Torihara. Because our reasoning regarding the rejection of claim 51 differs from the Examiner's, we designate our affirmance of the rejection of this claim as a New Grounds of Rejection.

We affirm the rejection of claims 28–30, 32–34, 41, 44, and 50 under 35 U.S.C. § 103(a) as unpatentable over Wang and Torihara. Because our reasoning regarding the rejection of claim 50 differs from the Examiner's, we designate our affirmance of the rejection of this claim as a New Grounds of Rejection.

We affirm the rejection of claims 35, 37, 42, and 43 under 35 U.S.C. § 103(a) as unpatentable over Wang, Torihara, and Panigrahi.

We affirm the rejection of claim 40 under 35 U.S.C. § 103(a) as unpatentable over Woeller, Torihara, and Panigrahi.

We affirm the rejection of claim 45 under 35 U.S.C. § 103(a) as unpatentable over Woeller, Torihara, and Wang.

TIME PERIOD FOR RESPONSE

37 C.F.R. § 41.50(b) also provides that the Appellants, WITHIN TWO MONTHS FROM THE DATE OF THE DECISION, must exercise one of the following two options with respect to the new grounds of rejection to avoid termination of the appeal as to the rejected claims:

> (1) *Reopen prosecution*. Submit an appropriate amendment of the claims so rejected or new Evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the prosecution will be remanded to the examiner. . . .
>
> (2) *Request rehearing*. Request that the proceeding be reheard under § 41.52 by the Board upon the same Record. . . .

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED, 37 C.F.R. § 41.50(b)